

WHAT IS CLAIMED IS:

1. A process of treating oral leukoplakia lesions of humans in need of such treatment, the process comprising the step of applying topically to the leukoplakia lesion an effective amount of a clear aqueous formulation comprising:

water;

a water miscible pharmaceutically acceptable polyol;

a pharmaceutically acceptable unsaturated fatty acid ester;

a pharmaceutically acceptable surfactant, and

β -carotene, said β -carotene being in a micellized form within said formulation.

2. A process in accordance with Claim 1 wherein the formulation additionally comprises a pharmaceutically acceptable anti-oxidant.

3. A process in accordance with Claim 2 wherein the pharmaceutically acceptable anti-oxidant is d-alpha-tocopherol or a pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E activity.

4. A process in accordance with Claim 1 wherein the formulation additionally comprises a compound having vitamin A activity.

5. A process in accordance with Claim 1 wherein the surfactant is polyethoxylated castor oil.

1 6. A process in accordance with Claim 1 wherein the polyol is
2 glycerol.

3 7. A process in accordance with Claim 1 wherein the unsaturated fatty
4 acid ester is ethyl linoleate.

5 8. A process in accordance with Claim 1 wherein the formulation is a
6 gel.

7 9. A process in accordance with Claim 8 comprising the steps of
8 applying the gel to the leukoplakia lesion at least twice a day.

9 10. A process in accordance with Claim 1 wherein the formulation
10 comprises:

11 10 to 50 % by weight water;

12 5 to 40 % by weight of the water miscible pharmaceutically acceptable
13 polyol;

14 1 to 20 % by weight of the pharmaceutically acceptable unsaturated
15 fatty acid ester;

16 10 to 60 % by weight of the pharmaceutically acceptable surfactant,
17 and

18 0.03 to 9.0 % by weight of β -carotene.

19 11. A process in accordance with Claim 10 wherein the water miscible
20 pharmaceutically acceptable polyol is glycerol;

1 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl
2 linoleate, and

3 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

4 12. A process in accordance with Claim 1 wherein the formulation
5 comprises:

6 20 to 40 % by weight water;

7 10 to 30 % by weight of the water miscible pharmaceutically
8 acceptable polyol;

9 1 to 15 % by weight of the pharmaceutically acceptable unsaturated
10 fatty acid ester;

11 20 to 40 % by weight of the pharmaceutically acceptable surfactant,
12 and

13 0.3 to 3.0 % by weight of β -carotene.

14 13. A process in accordance with Claim 12 wherein the water miscible
15 pharmaceutically acceptable polyol is glycerol;

16 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl
17 linoleate, and

18 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

19 14. A process in accordance with Claim 13 wherein the formulation
20 additionally comprises d-alpha-tocopherol and a compound having vitamin A

1 activity.

2 15. A process in accordance with Claim 14 wherein the formulation is
3 a gel.

4 16. A process in accordance with Claim 15 comprising the steps of
5 applying the gel to the leukoplakia lesion at least twice a day.

6 17. A process in accordance with Claim 1 wherein the formulation
7 comprises:

8 50 to 95 % by weight water;

9 1 to 10 % by weight of the water miscible pharmaceutically acceptable
10 polyol;

11 0.01 to 2 % by weight of the pharmaceutically acceptable unsaturated
12 fatty acid ester;

13 0.01 to 5 % by weight of the pharmaceutically acceptable surfactant,
14 and

15 0.003 to 1.2 % by weight of β -carotene,

16 1 to 10 % by weight of a pharmaceutically acceptable sweetener;

17 0.01 to 2% of a pharmaceutically acceptable antibacterial agent;

18
19 d -alpha tocopherol or a pharmaceutically acceptable derivative of d-
20 alpha tocopherol having vitamin E activity;

1 vitamin A palmitate or a pharmaceutically acceptable derivative of
2 vitamin A palmitate having vitamin A activity;
3 a pharmaceutically acceptable chelating agent;
4 a pharmaceutically acceptable antifoaming agent;
5 a flavoring agent, and
6 a preservative.

7 18. A process in accordance with Claim 17 wherein the water miscible
8 pharmaceutically acceptable polyol is glycerol;

9 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl
10 linoleate;

11 the pharmaceutically acceptable surfactant is polyethoxylated castor
12 oil;

13 the pharmaceutically acceptable sweetener is xylitol;

14 the pharmaceutically acceptable antibacterial agent is cetyl pyridinium
15 chloride;

16 the pharmaceutically acceptable chelating agent is disodium EDTA,
17 and

18 the preservative is sodium benzoate.

19 19. A process in accordance with Claim 18 wherein the formulation is
20 an oral rinse.

1 **20.** A process in accordance with Claim 19 wherein the formulation
2 comprises:

3 75 to 95 % by weight water;
4 2 to 7 % by weight of glycerol;
5 0.01 to 0.5 % by weight ethyl linoleate;
6 0.01 to 1 % by weight polyethoxylated castor oil;
7 0.003 to 10.6 % by weight of β -carotene,
8 2 to 7 % by weight of xylitol;
9 0.01 to 1 % of cetyl pyridinium chloride;
10 0.005 to 0.05 % by weight of disodium EDTA;
11 0.2 to 1.5 % by weight of flavoring agent, and
12 0.01 to 0.5 % by weight of sodium benzoate.

13 **21.** A clear aqueous composition for topical application in the oral
14 cavity of humans, the composition comprising:
15 water;
16 a water miscible pharmaceutically acceptable polyol;
17 a pharmaceutically acceptable unsaturated fatty acid ester;
18 a pharmaceutically acceptable surfactant, and
19 β -carotene, said β -carotene being in a micellized form within said
20 composition.

1 22. A composition in accordance with Claim 21 wherein the
2 composition additionally comprises a pharmaceutically acceptable anti-
3 oxidant.

4 23. A composition in accordance with Claim 22 wherein the
5 pharmaceutically acceptable anti-oxidant is d-alpha-tocopherol or a
6 pharmaceutically acceptable derivative of d-alpha tocopherol having vitamin E
7 activity.

8 24. A composition in accordance with Claim 21 wherein the
9 composition additionally comprises a compound having vitamin A activity.

10 25. A composition in accordance with Claim 21 wherein the surfactant
11 is polyethoxylated castor oil.

12 26. A composition in accordance with Claim 21 wherein the polyol is
13 glycerol.

14 27. A composition in accordance with Claim 21 wherein the
15 unsaturated fatty acid ester is ethyl linoleate.

16 28. A composition in accordance with Claim 21 wherein the
17 composition is a gel.

18 29. A composition in accordance with Claim 21 wherein the
19 composition comprises:

20 10 to 50 % by weight water;

1 5 to 40 % by weight of the water miscible pharmaceutically acceptable
2 polyol;
3 1 to 20 % by weight of the pharmaceutically acceptable unsaturated
4 fatty acid ester;
5 10 to 60 % by weight of the pharmaceutically acceptable surfactant,
6 and
7 0.03 to 9.0 % by weight of β -carotene.

8 **30.** A composition in accordance with Claim 29 wherein the water
9 miscible pharmaceutically acceptable polyol is glycerol;
10 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl
11 linoleate, and
12 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

13 **31.** A composition in accordance with Claim 21 wherein the
14 composition comprises:

15 20 to 40 % by weight water;
16 10 to 30 % by weight of the water miscible pharmaceutically
17 acceptable polyol;
18 1 to 15 % by weight of the pharmaceutically acceptable unsaturated
19 fatty acid ester;
20 20 to 40 % by weight of the pharmaceutically acceptable surfactant,
21 and

1 0.3 to 3.0 % by weight of β -carotene.

2 **32.** A composition in accordance with Claim 31 wherein the water
3 miscible pharmaceutically acceptable polyol is glycerol;
4 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl
5 linoleate, and
6 the pharmaceutically acceptable surfactant is polyethoxylated castor oil.

7 **33.** A composition in accordance with Claim 32 wherein the
8 composition additionally comprises d-alpha-tocopherol and a compound
9 having vitamin A activity.

10 **34.** A composition in accordance with Claim 33 wherein the
11 composition is a gel.

12 **35.** A composition in accordance with Claim 21 wherein the
13 composition comprises:

14 50 to 95 % by weight water;

15 1 to 10 % by weight of the water miscible pharmaceutically acceptable
16 polyol;

17 0.01 to 2 % by weight of the pharmaceutically acceptable unsaturated
18 fatty acid ester;

19 0.01 to 5 % by weight of the pharmaceutically acceptable surfactant,
20 and

1 0.003 to 1.2 % by weight of β -carotene,
2 1 to 10 % by weight of a pharmaceutically acceptable sweetener;
3 0.01 to 2% of a pharmaceutically acceptable antibacterial agent;
4 d -alpha tocopherol or a pharmaceutically acceptable derivative of d-
5 alpha tocopherol having vitamin E activity;
6 vitamin A palmitate or a pharmaceutically acceptable derivative of
7 vitamin A palmitate having vitamin A activity;
8 a pharmaceutically acceptable chelating agent;
9 a pharmaceutically acceptable antifoaming agent;
10 a flavoring agent, and
11 a preservative.

12 36. A composition in accordance with Claim 35 wherein the water
13 miscible pharmaceutically acceptable polyol is glycerol;

14 the pharmaceutically acceptable unsaturated fatty acid ester is ethyl
15 linoleate;

16 the pharmaceutically acceptable surfactant is polyethoxylated castor
17 oil;

18 the pharmaceutically acceptable sweetener is xylitol;

19 the pharmaceutically acceptable antibacterial agent is cetyl pyridinium
20 chloride;

21 the pharmaceutically acceptable chelating agent is disodium EDTA,

1 and

2 the preservative is sodium benzoate.

3 37. A composition in accordance with Claim 36 wherein the
4 composition is an oral rinse.

5 38. A composition in accordance with Claim 37 wherein the
6 composition comprises:

7 75 to 95 % by weight water;

8 2 to 7 % by weight of glycerol;

9 0.01 to 0.5 % by weight ethyl linoleate;

10 0.01 to 1 % by weight polyethoxylated castor oil;

11 0.003 to 10.6 % by weight of β -carotene,

12 2 to 7 % by weight of xylitol;

13 0.01 to 1 % of cetyl pyridinium chloride;

14 0.005 to 0.05 % by weight of disodium EDTA;

15 0.2 to 1.5 % by weight of flavoring agent, and

16 0.01 to 0.5 % by weight of sodium benzoate.

17 39. A clear aqueous gel composition for topical application in the oral
18 cavity of humans, the composition having been prepared by a process
19 comprising the steps of:

20 admixing a suspension of β -carotene in edible oil with polyethoxylated

1 castor oil and heating said admixture to approximately 160 to 180 °C and
2 agitating said admixture in said temperature range of 160 to 180 °C until a
3 clear homogeneous solution is obtained;

4 thereafter cooling said admixture to approximately 130 to 135 °C and
5 adding d-alpha-tocopherol, glycerol and ethyl linoleate to said admixture, the
6 d-alpha-tocopherol, glycerol and ethyl linoleate being added to the admixture
7 at such a rate of addition that the temperature of the resulting mixture is
8 cooled to approximately 85 to 95 ° C;

9 maintaining the resulting mixture under agitation at 85 to 95° C until a
10 clear homogeneous mixture is obtained;

11 thereafter adding under agitation water of approximately 55 to 60°C
12 temperature and cooling the mixture under agitation until a clear homogenous
13 product is obtained.

14 **40.** A clear aqueous gel composition in accordance with Claim 39
15 comprising:

16 20 to 40 % by weight water;

17 10 to 30 % by weight of glycerol;

18 1 to 15 % by weight of ethyl linoleate;

19 20 to 40 % by weight of polyethoxylated castor oil;

20 0.3 to 3.0 % by weight of β -carotene.